DOCKET NO.: ISIS-3070 **Application No.:** 09/424,521 **Office Action Dated:** July 2, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

Amendments to the Specification:

Please amend the paragraph that was added at page 1, line 3 by the November 2, 2000 amendment as follows.

This patent application derives from International Patent Application PCT/US98/10804, filed on May 28, 1998, which claims priority to application Serial No. 08/864,765, filed on May 28, 1997 (now abandoned), which is a continuation-in-part of application Serial No. 08/595,387, filed on February 1, 1996 (now U.S. Patent No. 5,773,571), which is a continuation-in-part of application Serial No. 08/054,363, filed on April 26, 1993 (now U.S. Patent No. 5,539,082); this patent application is also a continuation-in-part of application Serial No. 08/108,591, filed on November 22, 1993 (now U.S. Patent No. 6,395,474), which derives from International Patent Application PCT/EP92/01219, filed on May 22, 1992, published as WO92/20702.

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